Epithelium

**I. Introduction**

A. Definitions

1. Levels of Organization

**Cells**: Basic unit of all animals, over 200 types of cells in body.

**Tissues**: Group of similar cells grouped together to perform a

specific function.

**Organs:** Two or more tissues grouped together to perform a

specific function.

**Systems:** Two or more organs that work together to perform

a specific function.

2. Four Basic Tissue Types

a. **Epithelium:** A layer of cells that covers the body's surfaces.

Selective barrier to aid or prevent materials from traversing

the surface they cover.

b. **Muscle:** A group of cells that change shape, specialized for

contraction. Responsible for locomotion, constriction, pumping,

& peristalsis.

c. **Nerve:** A group of cells characterized by their excitability. Receptors

receive stimuli and transform that into an impluse that is carried to

the brain where it is interpreted.

Organism can react to the stimuli.

Two cell types: neurons and neuroglia cells.

d. **Connective Tissue:** A group of cells that connects the other tissues

together in the body. Connects the cells both structurally and

metabolically.

*Blood vessels must pass through connective tissue*

Relatively few cells, large amount of extracellular matrix between the

cells.

B. Common Structure of Epithelium

Look closer at the implications of the definition of epithelium

Characteristics of epithelia- dozen or more specific types

1. Predominantly cellular - contiguous sheet of cells that forms layers/membranes

2. Numerous intercellular junctions

3. Polar cells - Has **basolateral** and **apical** portions of cell & membrane

4. Free surface – apical surface, no other tissues there

5. Sits on basement membrane of connective tissue

6. Avascular - receives nutrients from the connective tissue it sits on

C. Embryological Origin:

Epithelia are derived from the three germ layers of the embryo

1. Ectoderm gives rise to epidermis

2. Endoderm gives rise to the linings of the GI tract, respiratory tract, and distal

parts of the urogenital tract

3. Mesoderm gives rise to the linings of internal cavities of the body.

**Mesothelium** lines the pericardial, pleural and peritoneal cavities

**Endothelium** lines the blood & lymphatic vessels and heart

D. Functions of Epithelia

1. Function as selectively permeable barriers – like a macro PM

Aid or prevent materials from traversing the surface they cover

2. Protection against:

Mechanical damage – skin protects against cuts

Dehydration damage – skin keeps in water

Chemical damage – skin protects against various chemicals

3. Secretion:

Produce and secrete materials in to spaces they bound

Glands are part of epithelium basic tissue type – all derived from epithelium

4. Absorption: e.g. GI tract

5. Transport: e.g. endothelium, lung

6. Function as sensory surface

Numerous receptors for touch, pain, temperature, taste, hearing

7. Can regenerate and repair itself

**II. Classification of Epithelium By Structure**

Two parts to name of each epithelium

Classified by two characteristics:

1. Number of layers of cells

**Unilaminar** - single layer = **simple**

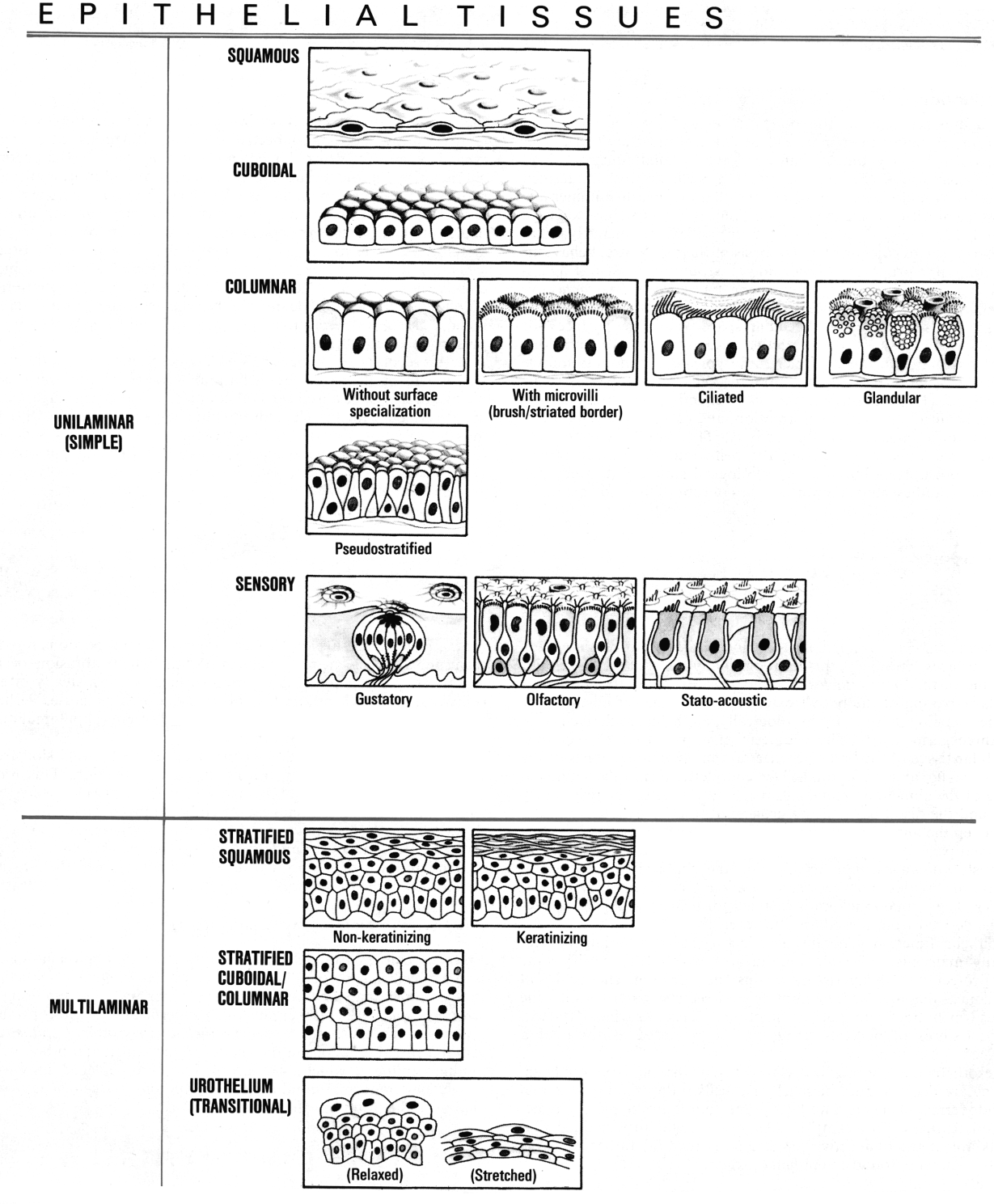
**Multilaminar** - more than one layer = **stratified**

2. Shape of cell

**Squamous** - thin flatten cells

**Cuboidal** - cells are a cube

**Columnar** - tall narrow cells



**SIMPLE:**

Single layer of cells – easy for molecules/cells to pass through when needed

– nutrient absorption/cell migration

**A. Simple squamous epithelium**: e.g. endothelium of blood & lymphatic vessels ,

mesothelium of peritoneal cavity

**B. Simple cuboidal epithelium**: e.g. ducts of glands, covering of ovary, kidney

tubules

**C. Simple columnar epithelium**: e.g. GI tract, gall bladder, parts of reproductive

tract uterus, efferent ductules, part of respiratory tract bronchioles

**D. Pseudostratified columnar epithelium**

Appears stratified because *nuclei* are located at different levels within the

epithelium

All cells reach the basement membrane

Some cells are tall and some are short with nuclei at different levels

All cells do not reach surface

e.g. Most of respiratory tract, trachea, epididymis, nasal cavity,

**STRATIFIED:**

Multilaminar/Stratified Epithelium = more than one layer, more protective

*Based on shape of cell at surface\**

**A. Stratified Squamous Epithelium:**

Principal type of stratified epithelium

TWO types: **keratinized** and **non-keratinized**

Multiple layers of cells

Deepest layer rests on basement membrane

Varying shapes of cells as they migrate to surface

**B. Keratinized Stratified Squamous Epithelium:**

Contains fibrous protein called keratin

Kills cells as migrate upward - killed by the accumulation of keratin

*No nuclei in surface layers \* Diagnostic*

e.g. epidermis of skin

**C. Non-keratinized Stratified Squamous Epithelium:**

Has same appearance as keratinized

Nuclei in surface cells \*Diagnostic

e.g. wet (mucosal) inner surfaces, oral cavity, esophagus, vagina, conjunctiva of eye

AKA: ***Stratified Squamous Mucosal Epithelium***

**D. Stratified Cuboidal Epithelium:**

Two layers of cuboidal shaped cells

e.g. ducts of sweat glands, pancreas, salivary glands

**E. Transitional Epithelium (Uroepithelium):**

Thought to be in transition between stratified cuboidal and stratified squamous

Lines most of the urinary tract (not kidney) hence other name of uroepithelium

Different appearance in distended and relaxed conditions

Undergoes considerable stretching, structure allows for this

**Non-distended uroepithelium:**

Many layers of cells (5-10)

Surface cells are large dome-shaped cells (cuboidal)

Tight junctions keep urine from leaking out of bladder

Membrane folded up and forms plaques in cytoplasm

**Distended Uroepithelium:**

Only 3-4 layers thick

Surface cells are squamous

**SPECIALIZED EPITHELIUM:**

These do not fall cleanly into the above categories

Classified as either **sensory** or **germinal**

*Based on specialized functions*

**A. Sensory Epithelium:**

**1. Gustatory**: covers tongue; contain taste buds

**2. Olfactory**: covering part of nasal passage way

contains neuroepithelial cells; the sense smell

**3. Stato-acoustic**: covering inner ear (choclear duct & portion semicircular

canals); senses sound & proprioception

**B. Germinal Epithelium**

Lines seminiferous tubule of testis; produce reproductive cells

**III. Polarity of Epithelium**

Epithelial cells have different morphological, functional and biochemical domains

Gives the cells and epithelium polarity

**Domains:**

Morphologically divided into **apical domain** and **basolateral domains**

Each domain has its own structural and functional differences in membranes and

surface specializations.

**A. Apical Domain:**

Free surface (luminal) side of cell

Plasma membrane contains different proteins than that of the basolateral domain

Membrane contains:

Carrier proteins

Glycoproteins

Carbohydrates attached to transmembrane proteins

Forms **glycocalyx (cell coat)**

Important in cell recognition and cell adhesion

Hydrolytic enzymes

Aquaporins

Channel forming proteins that function in the balance of water within the cell.

Capable of **endocytosis, exocytosis and transcytosis**

**Endocytosis** - material entering into cell

Formed from coated pit in membrane with **clathrin** on inside of membrane.

Pinched off to form **coated vesicle** within cytoplasm forms

**endosome** by losing its clathrin coat.

**Receptor-Mediated Endocytosis**

Coated pit has specific membrane receptors that bind material

**Exocytosis** of material being secreted from the cell

Occurs at apical surface in exocrine glands

e.g. mucus or serous secretion of salivary gland

Occurs at basolateral surface in endocrine glands

**Transcytosis** - process of large molecules being transported from one

surface of the cell to the other

Usually thought of as apical to basolateral but can go in both

directions.

**Membrane Specializations: (Apical surface)**

Four surface modifications that help to carry out the function of apical

surface: **microvilli, stereocilia, cilia & flagella**

**1. Microvilli (non-motile)**

Small finger-like projections from apical surface

**Increase cell surface area** in regions where there are large amounts of fluids being absorbed

1-2 μm in length, closely packed together

Forms striated or brush border

Internal support consists of 25-30 actin filaments

Joined at tip of microvillus by protein **villin**

**Fimbrin** cross links actin filaments down length

Actin filament embed into the **terminal web** at the base of the

microvilli

Terminal web consists of actin and spectrin molecules as well as

intermediate filaments

Myosin I and calmodulin connect actin filaments at regular intervals

to the membrane

Acts to hold microvillus upright

Are NON-MOTILE

Located on lining cells of GI tract, prox. tubule of kidney

**2. Stereocilia** have same internal structure as

Microvilli, therefore name is misnomer

Size is only difference - very long microvilli - 40-80 μm

Located in epididymis (concentrates sperm)

**3. Cilia:**

Second apical surface specialization

Larger, 0.2 μm diameter, 7-10 μm length

Core consists of complex arrangement of microtubules

Core called **axoneme**

Are MOTILE - different from microvilli

Function is to propel mucus over the surface of the epithelium via rapid

rhythmic beating of the cilia

Location: Pseudostratified ciliated epithelium of respiratory tract

Attached to **basal body** in cytoplasm at base of cilium

9 triplets- different from axoneme (9+2 doublets)

How do cilia move?

Axoneme is responsible for motility.

Consists of longitudinally-oriented microtubules in a 9+2

arrangement

**2 singlets** (single microtubules) centrally located

Surrounded by **9 doublets** of microtubules

In cross section, a doublet consists of two subunits

**Subunit A** composed of 13 protofilaments arranged in a circle

**Subunit B** consists of 10 protofilaments in circular arrangement with

3 protofilament of subunit A completing the circle

**Sheath** surrounds the singlets

**Radial spoke** projects from Subunit A toward sheath

Composed of elastic proteins

Thought to prevent buckling when cilia bends

Neighboring doublets connected by another elastic protein, **nexin**

**Dynein,** a microtubule associated protein, projects two arms from

subunit A towards subunit B of adjacent doublet

Located at 24nm intervals along subunit A

**Dynein ATPase** provides energy to bend cilium

Causes dynein arms to transiently attach to subunit B of

adjacent doublet

Slides toward tip of cilium

Nexin (elastic protein) translates sliding motion into

bending motion

Dynein releases subunit B and snaps the cilium back upright

Beat of cilium

**Effector Stroke** -Cilium starts upright and bends

forward, moves mucus

**Recovery Stroke** ( preparatory)

Cilium returns to upright position

Beating of cilia is coordinated within a single cell and

between adjacent cells

Results in movement of fluid and particulate matter

in one direction along epithelial surface.

IMPORTANCE of motile cilia

Clinical syndrome called **primary ciliary dyskinesia** or **immotile**

**cilia syndrome** or **Kartagener's syndrome**

Stucturally lacking dynein cross arms or radial spokes

Results in immotile cilia

Patients can't clear respiratory tract, numerous lung infections,

infertile, malrotation of heart

**4. Flagella:**

Structurally very similar to cilium but larger with mitochondria wrapped

around the axoneme

**B. Basolateral Domain:**

Consists of the lateral sides and base of the epithelial cell

Membrane of each has own specialized cell junctions, hormone receptors,

Na+, K+, ATPase, ion channels

Lateral domain is characterized by the **junctional complex** AKA

**terminal bars**

Place where two cells contact or attach to each other near apical

surface (holds cells tightly together)

Runs in zone all away around the circumference of the cell

Consist of 3 different types of structural and functional attachments or

junctions:

Called **Zonula Occludens, Zonula Adherens** and **Macula Adherens**

**Junctions.**

1. **Zonula Occludens**: AKA **Tight Junctions**

Most superficial to apical surface

Creates impermeable barrier so materials cannot pass between

cells

Fusion of adjacent membranes by transmembrane proteins,

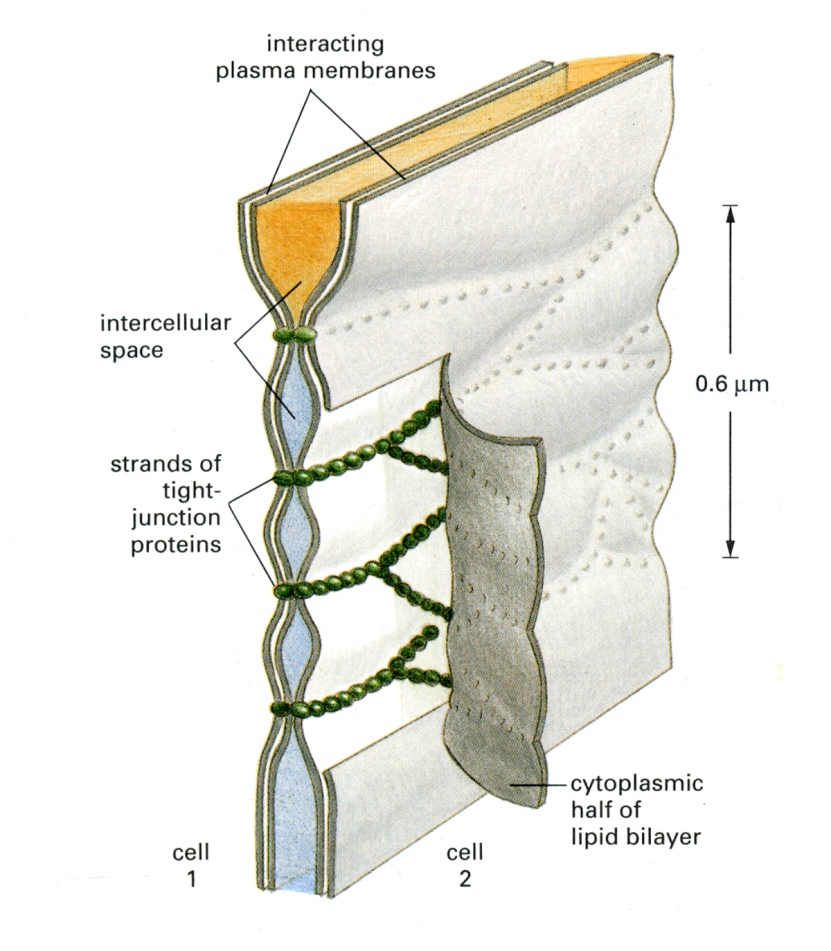
**claudin** and **occludin**

Arranged as **anastomosing strands**

Gives quilted appearance

Reinforced by **Cadherins,** another family of CAMs

Small molecules can still pass through plasma membrane

 Larger molecules cannot pass through the tight junctions

Function of Zonula Occludens;

Barrier function - makes epithelial sheet impermeable to

substances

"Tight" vs "leaky" occludens junctions

Marks division of apical and basolateral membranes

Prevents movement of membrane proteins from migrating

from one domain to the other

**2. Zonula Adherens:** AKA **Adhesion Belt**: incorrectly

called belt desmosome

Functions as mechanical attachment to adjacent cells

Mechanically holds the cells together

Also extends around circumference of each cell

More complex structure:

Intercellular gap between membranes,15-20nm

Transmembrane linker proteins called **Cadherin**

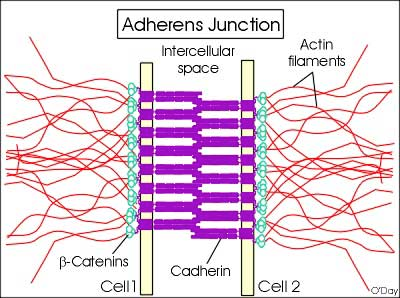
Extends across gap and holds membranes together

Cadherins bind to cell cytoskeleton

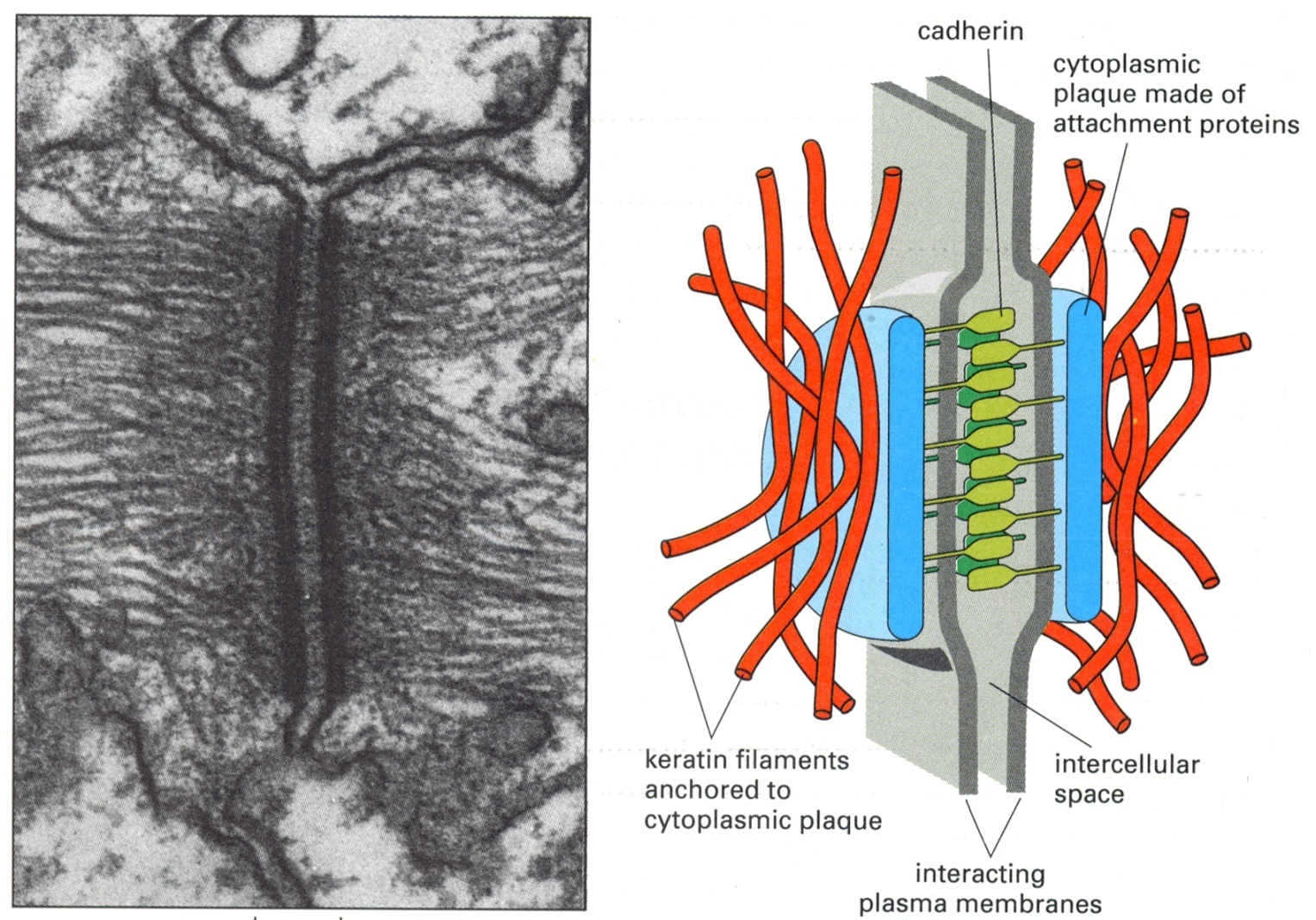
Dense aggregation of actin filaments

Linker proteins: **talin, vinculin** & **α-actinin**

bind actin filaments to cell membrane



**3. Macula Adherens** AKA **Desmosome**:



3rd junction & deepest in junctional complex

Also for mechanical attachment of adjacent cells

Structure: like a "spot weld" 🡪 mechanical attachment

Gap between adjacent membranes - 30μm

Dense **attachment plaques** on cytoplasmic side of each

membrane

Consist of **desmoplakin** & **plakoglobin**

Transmembrane proteins extend across gap that attaches 2

membranes

The cadherins: **desmoglein** and **desmocolin**

**Intermediate filaments** attach into attachment plaque

Clinical relevance:

**Phemphigus vulgaris**

Autoimmune disease

Antibodies to cadherin desmoglein

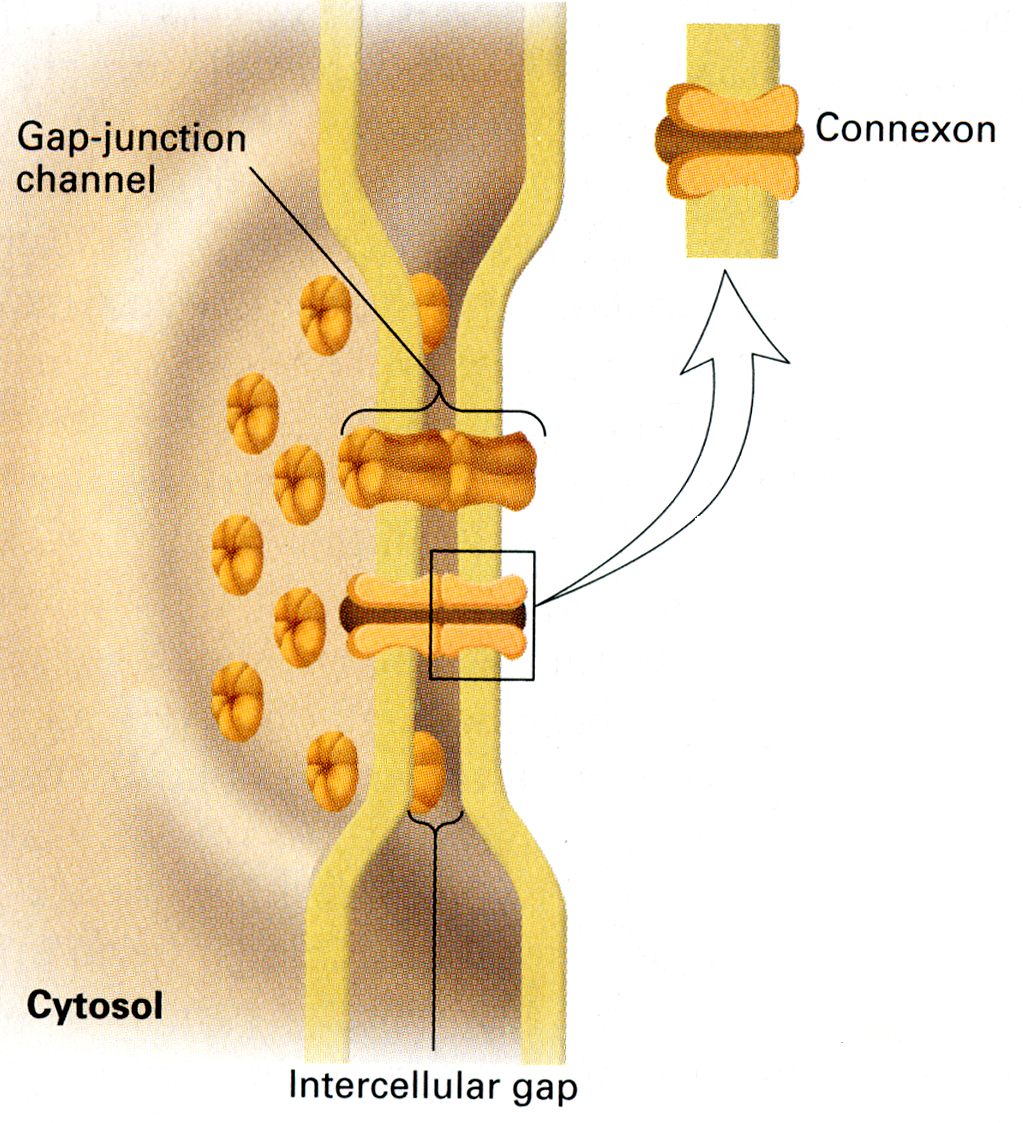
Patient desmosomes are destroyed, particularly in skin

Causes severe blistering due to water loss

Infections that are life threatening

Lateral domain also contains a fourth type of junction

**4. Gap Junction or Nexus**



Scattered throughout the lateral domain (not part of junctional complex)

Functions in cell to cell communication

Both electrically and metabolically

Cell membrane separated by 2-3 nm

Disc of numerous **connexons**

Aqueous pores in cell membrane extend about 1.5nm beyond

membrane

6 protein subunits, **connexin**, form a barrel-like channel from

cytoplasm of one cell to cytoplasm of adjacent cell

Connexon of one membrane must line up with connexon of adjacent

membrane

Forms 1.5nm diameter channel

Permits ions, small amino acids, c-AMP, nucleotides and some vitamins

Does **not** permit passage of proteins, nucleic acids and polysaccharides

Point of low electrical resistance

Can pass along electrical impulse for contraction of smooth muscle to

create a peristaltic wave in the gut

Distributes informational molecules during cell migration embryogenesis

**Basal Domain:**

Has 3 specialized structures that reflect its function:

**Basal lamina, membrane enfoldings** & **hemidesmosomes**

**1. Basal lamina**: a dense layer that is located just

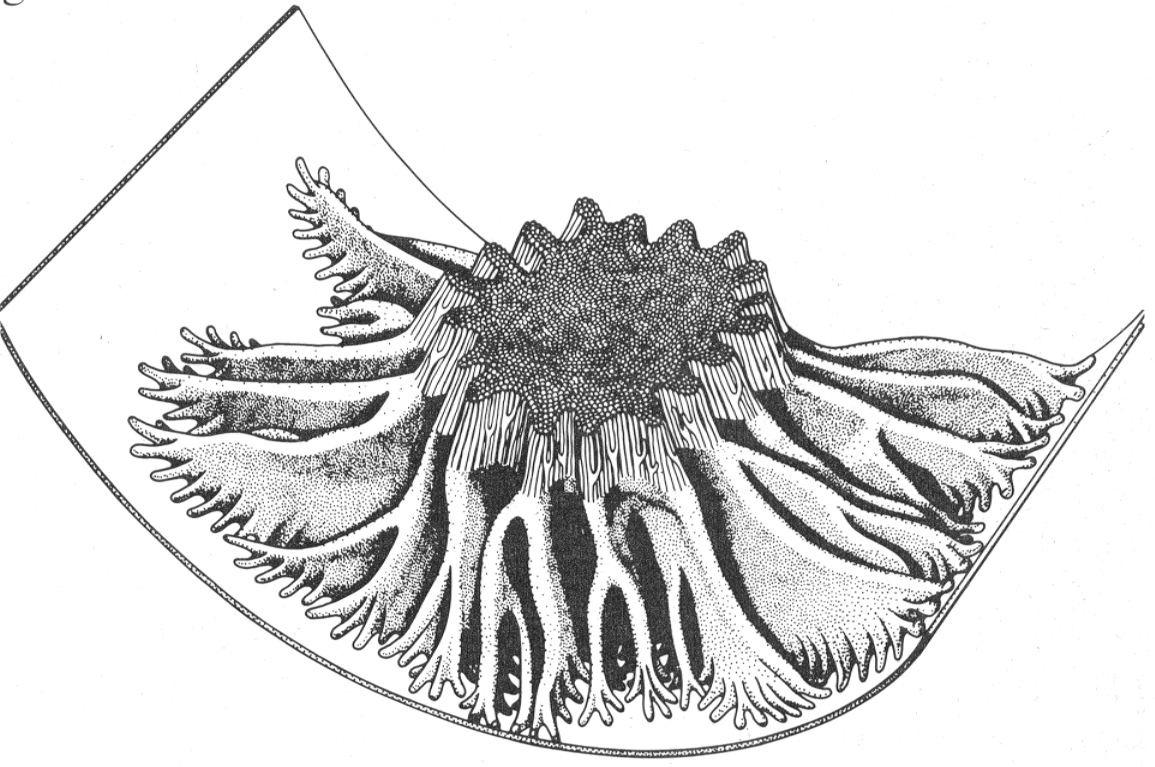
subadjacent (below) to the basal membrane

*in the extracellular matrix – holds cell to connective tissue*

**2. Plasma membrane enfoldings:**

Some epithelial cells have highly enfolded basal membrane (tesselated)

Increases SA for increased passage of fluids



3. Hemidesmosomes

Appears as half of a desmosome on cytoplasmic side

Intermediate filaments embedded into plaque

Transmembrane protein is **integrin**

Binds cell membrane to basement membrane and hence to underlying connective tissue

IV. GLANDS:

Are considered epithelium because they are formed as outgrowths of the epithelium

A.  **Exocrine** versus **Endocrine Glands: (with or without duct)**

If the connection to the surface epithelium remains to form a duct, then the gland is

an **exocrine gland**

The product of the gland is delivered to the epithelial surface

If the connection to the surface epithelium disintegrates and gland is without a duct,

then the gland is an **endocrine gland**

It secretes its product into the surrounding extracellular matrix where it is quickly transferred into the blood

All glands can be classified 3 different ways: by their ***structure, mode of secretion*** or **t*ype***

***of secretion*** produced

B. **Structural/Morphological Classification**:

**Unicellular** vs **Multicellular** Glands is the first structural characteristic

1. **Unicellular Glands**: consist of single cells embedded in epithelial layer

Eg.: Globlet cell - Secretes mucus directly onto the surface of the epithelium

**2. Multicellular Glands**: Consists of numerous cells and can be divided into a duct and

secretory portions

Named according to ***(1) branching of the duct system*** and ***(2) shape of the***

***secretory portion*** *\*\*Important*

**Duct portion:**

First part of name is based on *branching of duct*

Have choice of **simple** or **compound**

**Simple exocrine glands:**

Have single duct

**Compound exocrine glands:**

Have a multiple branched duct system

**Secretory portion:**

Second part of name is based on shape of secretory portion

Have choice of **tubular** or **acinar**

**Tubular:**

Secretory portion forms a long tube

**Acinar** or **Alveolar**:

Secretory portion in the shape of a grape

May have **myoepithelial** cells (basket cells) surrounding secretory portion

Characterized by long branching processes

Contractile to help extrude the secretion

Multicellular glands are surrounded by **connective tissue capsule**

Larger glands may have connective tissue septa that subdivides the gland

into lobes and lobules

Therefore can have the following structural types of glands:

**Simple tubular** eg: Gastric glands

**Simple alveolar** eg: Sebaceous glands of skin

**Simple branched alveolar** eg: Sebaceous glands

**Simple coiled tubular** eg: Sweat glands

**Compound tubuloalveolar** eg: Salivary glands, pancreas

**C. Classification by Mode of Secretion:**

Classified by the mechanism they secret their product from the cell

1. **Merocrine secretion**:

Exocytosis- secretory vesicle fuses with membrane and extrudes its contents

without loss of cytoplasm

*Most common form* of secretion

Eg's: sweat glands, salivary glands, pancreas, goblet cells, etc.

**2. Apocrine secretion:**

Secretion is pinched off of cell with part of cytoplasm & cell membrane lost

Eg: Lipid portion of milk of mammary gland

**Not** apocrine sweat gland (misnomer)

**3. Holocrine secretion:**

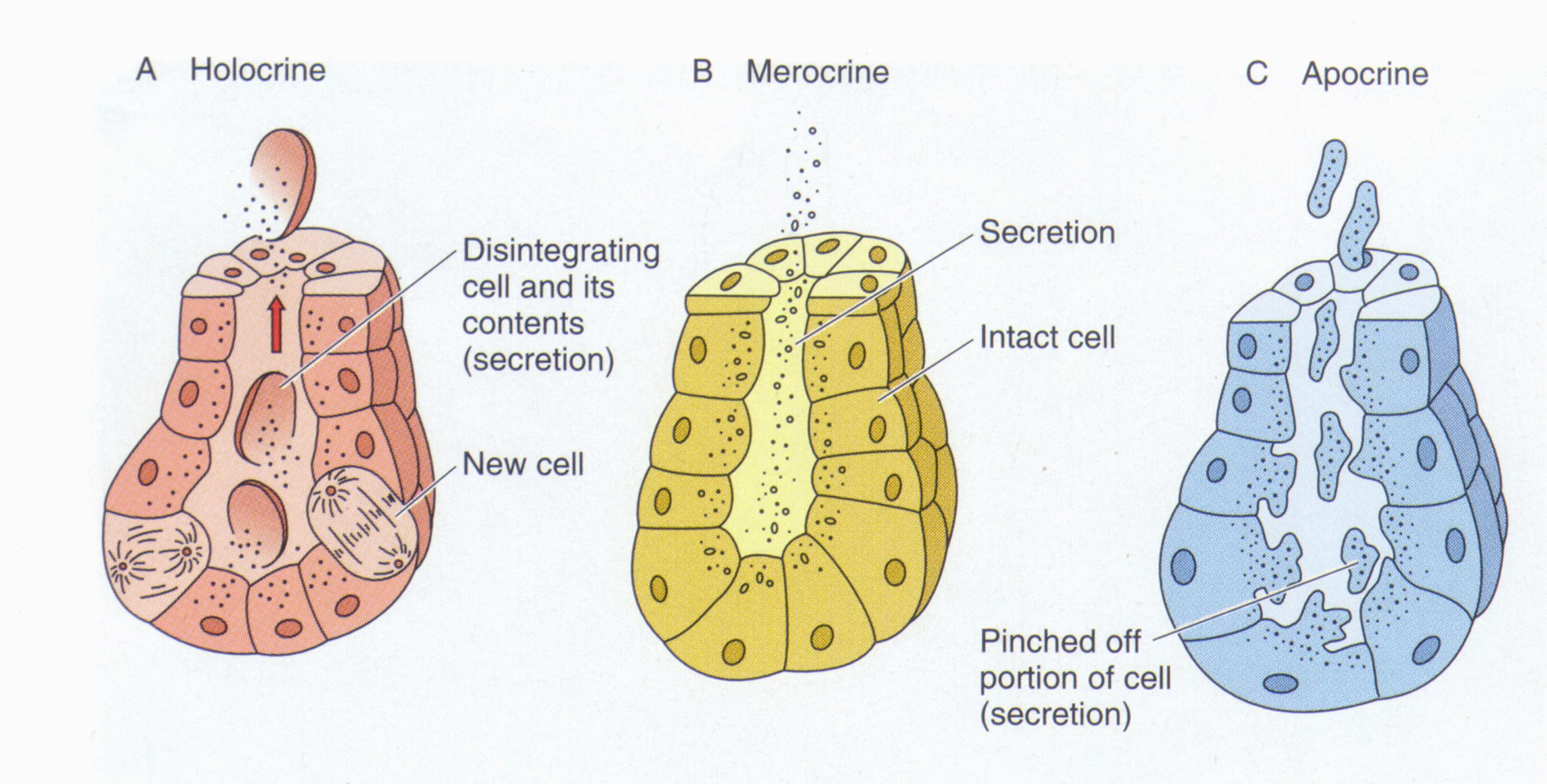
Cell fills up with secretion and dies

Degenerating cell forms secretion – secretion is essentially the dead cell

Eg: Sebaceous gland of skin

**4. Cytocrine secretion:**

Whole living cell is secreted

Eg's: ovary & testis (egg and sperm)

D. Classification by Type of Secretion:

The type of secretory product is the basis of this classification

1. **Mucus**:

Thick viscous secretion

Rich in **mucinogins**, large glycosylated proteins that take up large amounts of

water

Slippery; lubricant

Appears light staining with foamy cytoplasm due to extraction of mucus

Eg: goblet cell, sublingual salivary gland is mostly mucus

2. **Serous:**

Watery secretion

Could be rich in enzymes or ions

Cells appear acidophilic due to secretory machinery 🡪 stain darker than mucus

Eg's: pancreas, parotid or sweat glands

3. **Mixed glands**:

Combination of both serous and mucus secretions

Serous **demilunes**

Crescent or half moon on outside of mucus alveolus

Eg: salivary glands

4. **Sebum**:

Oily secretion

Rich in lipid

Lubricant

Eg’s: Sebaceous gland of skin, meibomian gland of eyelid

5. **Ceruminous:**

Waxy secretion

Protection

Eg: Ceruminous glands of external auditory canal